WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTÉ

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REPORT OF CONSULTATION ON THE JUSTIFICATION FOR RETENTION AND USE OF VARIOLA VIRUS IN THE POST ERADICATION ERA

1. Introduction

Transmission of endemic smallpox has apparently been interrupted all over the world, the last known case having occurred in Somalia in October 1977. It is anticipated that global eradication will be certified by December 1979. The potential danger of the retention of variola virus in laboratories was high-lighted by the occurrence of two cases of smallpox in Birmingham in August 1978. With these matters in mind the first meeting of the Global Commission for the Certification of Smallpox Eradication recommended that "an expert group to report to the Global Commission should be convened by WHO during 1979, to investigate whether retention of variola viruses is justified after global smallpox eradication has been completed, and if justified to identify the need for and nature of any research to be conducted".

The meeting was held in Geneva on 27-28 February 1979 and was attended by those listed in Annex 1.

Dr I.D. Ladnyi, Assistant Director-General of WHO, opened the meeting; Dr W.K. Joklik was designated Chairman and Dr F. Fenner, Rapporteur.

To provide background information, presentations were made on the current status of the global smallpox eradication programme, on laboratories retaining virus, on the situation relating to human monkeypox and monkeypox and whitepox viruses, and on the attitudes of the public and of scientists concerning the retention of variola virus. Documents available to the meeting are listed in Annex 2.

2. Matters considered by the Consultation

2.1 Whether further research work with variola virus* is justified.

2.2 If further research work is justified:

2.2.1 the kinds of research which should or should not be carried out;

2.2.2 what strains of variola virus should be retained, under what conditions and in what number and what kind of laboratories.

2.3 The time frame of the recommendations of the Consultation.

3. Background information related to recommendations of the Consultation

3.1 Possible animal reservoir of variola virus. The strategy and tactics of the Smallpox Eradication Programme have been based on the assumption that humans are the only reservoir of variola virus. In 1964 two strains of a virus indistinguishable from variola virus were

*Wherever variola virus is mentioned, it includes the so-called "whitepox" and "wild whitepox" viruses, which cannot be distinguished by any laboratory test from variola virus although their pathogenicity for man is unknown. (See also Report of the Workshop on Safety Measures in Laboratories Retaining Variola Virus (SME/77.2)).

recovered from monkey kidney cells in a diagnostic laboratory. These isolates were called "wild whitepox" (or "whitepox") viruses because of their pock-forming appearance on CAM, compared with monkeypox virus. Subsequently, four strains of "wild whitepox" virus were recovered from four different animals caught in the wild in Zaire between 1971 and 1975. All these strains, when subjected to a variety of laboratory tests, could not be distinguished from variola virus.

Another orthopoxvirus called monkeypox virus has been isolated from non-human primates in European and North American laboratories on ten separate occasions between 1958 and 1968. This virus is clearly distinguishable from variola virus by laboratory tests. Since 1970 it has been recognized that monkeypox virus can produce a disease in man clinically indistinguishable from smallpox. Thirty-seven cases of human monkeypox have been recognized in West and Central Africa between 1970 and 1978. The disease differs from smallpox in that it does not appear to spread easily between susceptible (non-vaccinated) humans.

In 1978 an investigator reported that viruses having many of the laboratory characters of whitepox virus could be isolated from cultures of monkeypox viruses. A consultation of expert virologists, meeting in November 1978, considered this finding and related issues and made specific recommendations pertaining to research with variola virus and related orthopoxviruses (SME/78.20).

3.2 Danger of retaining variola virus stocks. If there is no animal reservoir of variola virus, the only possible source of recurrence of smallpox is material held in laboratories. Some scientists and public health workers believed that this risk should be removed by the destruction of all stocks of variola virus.

3.3 Sites for retention of variola virus stocks. If variola virus is retained, there would be advantages in locating all variola virus stocks in a single laboratory, with maximum containment facilities. Research workers wishing to carry out experiments with variola virus would then have to do the work in that laboratory. There were practical difficulties in moving quickly to this situation, but the number of laboratories holding variola virus stocks should be reduced to the minimum number possible, as rapidly as possible.

3.4 Long-term need for "reference" strains of variola virus. Even if "whitepox virus" does not prove to be important as a potential animal reservoir of variola virus, other animal orthopoxviruses may become a threat to human health at some future time. Some scientists believed that "reference strains" of variola virus, or perhaps non-living material derived from variola virus, should be retained into the indefinite future to allow comparisons of such "new pathogens" with variola virus to be made.

3.5 Need to conserve variola virus for future scientific studies. Although most scientists agreed that currently no research other than work devoted strictly to promotion of the Smallpox Eradication Programme could be justified, it was impossible to forecast what future scientific discoveries might be made that would make it useful to carry out experimental studies with variola virus. Some scientists believed that strains of variola virus should therefore be retained for an indefinite period.

4. Recommendations

After careful consideration of the matters outlined above, the Consultation unanimously supported the following recommendations:

4.1 The Consultation agreed that the retention of variola virus stocks, even in maximum containment laboratories, carried a very small risk that further cases or outbreaks of smallpox could originate from such sources. This risk could be completely removed by the destruction of all stocks of variola virus. Nevertheless, the Consultation concluded that retention of stocks of variola virus for a period of up to three years from the time of its meeting could be justified on scientific grounds. The Consultation endorsed the recommendations for research on variola virus and related orthopoxviruses contained in the Report of the

Informal Consultation on Monkeypox, Whitepox and Related Poxviruses held on 9-10 November, 1978 (SME/78.20).

4.2 The Consultation recommended that not more than four laboratories retain variola virus stocks. Each such laboratory should be a WHO Collaborating Centre equipped with maximum containment facilities.

4.3 The Consultation recognized that national governments had the responsibility of ensuring safety in laboratories, but recommended that each laboratory retaining variola virus stocks should be inspected at intervals of no more than two years by WHO staff and consultants, who would evaluate their safety in terms of WHO guidelines.

4.4 The Consultation recommended that WHO should convene a meeting of scientists to decide which strains of virus should be retained. All strains not specifically recommended for retention should be destroyed. WHO should maintain a full inventory of all retained variola virus strains.

4.5 The Consultation recommended that the situation concerning retention of variola virus should be regularly reviewed by a group of experts convened by WHO. The first such review should be conducted not later than February 1982.

4.6 The Consultation recommended that research with variola virus should be restricted to studies that are of direct value to the Smallpox Eradication Programme (including research related to a possible animal reservoir of variola virus), and should be subject to advice and approval of an expert group appointed by WHO.

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DOCUMENTS AVAILABLE TO THE CONSULTATION

1. Monkeypox and Whitepox Viruses in West and Central Africa
   Bull. World Health Organ. Vol.53, 1976

2. Report of the First Meeting of the Global Commission for the Certification of Smallpox Eradication
   WHO/SE/78.132

3. Laboratories with Variola Virus Stocks
   Global Commission Working Paper 78.46

4. Post-Eradication Strategy: Virological Aspects
   Global Commission Working Paper 78.51

5. Report of Informal Consultation on Monkeypox, Whitepox and Related Poxviruses
   Global Commission Working Paper 78.48B (SME/78.20)

6. Laboratory Aspects of the Monkeypox Virus/Whitepox Virus Problem
   Global Commission Working Paper 78.48A

7. White Variants derived from Poxviruses
   Informal Consultation on Monkeypox, Whitepox and Related Poxviruses, WP5

8. Human Monkeypox: Update 1978
   Global Commission Working Paper 78.47

9. Comments by Dr D. Nathans, The Johns Hopkins University, Baltimore, USA

10. Extract from the New York Times Magazine
    (A view by a reporter 4 February 1979)

11. Terms of Reference of this Consultation; and Related Recommendations of the Global Commission (F.F)

12. Matters for Consideration and Recommendation (F.F)

13. Diagram: Genome maps of vaccinia, red cowpox and white cowpox viruses; from an article by L.C. Archard and M. Mackett (in press)

14. Possible Needs for Variola Virus in Diagnosis and Research (F.F)

15. Background Information on the Recovery of "Whitepox" viruses (F.F)

16. Weekly Epidemiological Record, No.1, 1979, pp.1-6

17. Report of a Workshop Meeting on Safety Measures in Laboratories Retaining Variola Virus
    SME/77.2